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Metabolic Syndrome and Thyroid Disease Spectrum

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Abstract **Background:** Metabolic syndrome is a group of abnormalities that in conjunction, substantially increase the risk of developing cardiovascular disease and type 2 diabetes. Thyroid disorders are often faced in clinical practice affecting up to 10% of older adults and, consequently, have been linked to several adverse health outcomes, including increased risk of cardiovascular events, both in their subclinical and overt condition. Despite this significance, limited data exists regarding the prevalence and characteristics of thyroid dysfunction and structure among Iraqi patients with metabolic syndrome. **Aim of Study:** To investigate structural (by ultrasound) and functional thyroid abnormalities in individuals diagnosed with metabolic syndrome. **Method:** The case-control study was conducted at Rizgary Teaching Hospital from June 2024 to January 2025. The study included 50 patients who meet the criteria for metabolic syndrome, defined according to the International Diabetes Federation (IDF) criteria, an additional 50 age- and sex-matched controls without metabolic syndrome were included. Thyroid function tests and thyroid ultrasounds were performed for the participants. **Result:** The statistical analysis yielded a p-value of 0.008, indicating a significant association between thyroid status and the presence of metabolic syndrome. The difference in triglyceride levels across thyroid dysfunction groups was statistically significant ($p = 0.02$). There is a statistically significant association between thyroid nodules and metabolic syndrome, $p<0.05$. **Conclusion:** There is a higher prevalence of both structural and functional thyroid dysfunction among metabolic syndrome patients. The serum level of triglyceride was higher in hypothyroidism patients. These findings emphasize the significance of routine thyroid evaluation in the management of metabolic syndrome to optimize cardiovascular risk and detect thyroid disease in its early stages.

Key Words Metabolic Syndrome, Thyroid Function, Hypothyroidism, Obesity

INTRODUCTION

Non-communicable diseases remain the leading cause of mortality worldwide, accounting for more than 41 million deaths annually, surpassing all other causes combined [1,2]. Among them diabetes mellitus and cardiovascular disease arose as major contributors which share multiple modifiable risk factors such as poor dietary choices, obesity, hypertension, dyslipidemia, and physical inactivity [2].

Metabolic syndrome is a cluster of inter-linked metabolic abnormalities, which collectively increase the risk of cardiovascular disease and type 2 diabetes [3,4]. Central abdominal obesity, elevated triglycerides, reduced high-density lipoprotein cholesterol (HDL-C), hypertension, and impaired glucose represent some of these metabolic abnormalities [5,6]. Currently, it is estimated that one quarter of the world's population is affected by metabolic syndrome, largely driven by the increasing rates of obesity [7,8]. According to the National Health and Nutrition Examination Survey (NHANES III), metabolic syndrome was present in 5% of individuals with normal weight, 22% of those who were overweight and 60% of individuals who were obese [9].

Beyond the established cardiovascular risks, metabolic syndrome has also been linked to disturbances in several endocrine pathways [10-12]. One such condition is thyroid dysfunction, which is among the most common endocrine disorders, affecting up to 10% of adults worldwide [13,14]. Thyroid hormones play a vital role in glucose and metabolism, as well as energy expenditure regulation [15]. Disturbances in the delicate balance maintained by these hormones, whether overt or subclinical, can influence body weight, blood pressure, and lipid profiles-many of the key components of metabolic syndrome [16]. Several studies

have observed a higher rate of functional and structural thyroid abnormalities among individuals with metabolic syndrome, hinting at a potentially bidirectional relationship [17,18]. To that end, insulin resistance has been linked to thyroid tissue changes and thyroid dysfunction has been found to worsen pre-existing metabolic derangements [19,20]. However, the strength of this association remains in doubt due to the inconsistencies across populations [21].

As such, we hypothesized that patients with metabolic syndrome have a higher prevalence of both functional and structural thyroid anomalies. In Iraq, where obesity and cardiovascular disease continue to be a burden, there is a lack of sufficient data regarding thyroid dysfunction in patients with metabolic syndrome. Exploring this relationship could prove to be essential in developing early detection and management strategies.

Aim of the Study

The study aims investigate thyroid structure and functional abnormalities in individuals diagnosed with metabolic syndrome.

Objectives of the Study

- To evaluate serum levels of thyroid function markers (TSH, Free T4, and Free T3) in patients with metabolic syndrome and compare them with a control group
- To examine the association between individual components of metabolic syndrome (abdominal obesity, high triglycerides, low HDL cholesterol, elevated blood pressure, and high fasting glucose) and thyroid function parameters
- To assess the prevalence of structural thyroid abnormalities (e.g., nodules on ultrasound) in patients with metabolic syndrome compared with controls
- To assess the influence of lifestyle and clinical factors (such as smoking, medication use, and prior thyroid disease) on thyroid function and structure in patients with metabolic syndrome
- To compare baseline demographic and clinical characteristics between the metabolic syndrome group and the control group

Rationale

Based on the fact that thyroid abnormalities are common in this locality and due to possible associations with metabolic syndrome as well as limited and infrequent studies have been performed in researchers' area, all provided the researchers the motivation to carry out his work.

METHODOLOGY

Study Design

This study is a cross-sectional study designed to investigate the structural and functional abnormalities of the thyroid gland in individuals diagnosed with metabolic syndrome. This design allows for assessing the relationship between metabolic syndrome and thyroid dysfunction at a single point in time.

Study Setting

The study was conducted at Rizgary Teaching Hospital, a tertiary care facility which is located in Erbil, Iraq. The data collection is scheduled from Jun 2024, to January 2025.

Participants

Inclusion Criteria: The study included 50 patients who meet the criteria for metabolic syndrome, defined according to the International Diabetes Federation (IDF) criteria, which require the presence of at least three of the following components and they are as follow:

- **Abdominal Obesity:** Waist measurements exceeding 102 cm for males and 88 cm for females
- **Triglycerides Increased:** Triglyceride levels in the serum are at least 150 mg/dL, or receiving drug therapy for hypertriglyceridemia
- **Decreased HDL Cholesterol:** For men, HDL cholesterol is below 40 mg/dL, and for women, it is below 50 mg/dL, or receiving drug therapy for low HDL
- **High Blood Pressure:** Systolic blood pressure is 130 mmHg or higher, or diastolic blood pressure is 85 mmHg or higher
- **Elevated Fasting Glucose:** Fasting plasma glucose levels equal to or greater than 100 mg/dL, or receiving drug therapy for hyperglycemia

Exclusion Criteria

Patients were excluded from the study if they had:

- Chronic liver disease
- Chronic kidney disease
- Congestive heart failure
- Pregnant ladies
- Women using oral contraceptives pills, glucocorticoids, amiodarone and lithium, that may affect thyroid function tests

An additional 50 individuals without any criteria for metabolic syndrome were included as a control group. This group were served as a baseline for the comparison of thyroid function and structure. Controls were selected from individuals attending hospital for routine health checks who did not meet the criteria of metabolic syndrome. Both were matched approximately for age and sex to minimize confounding.

Data Collection

Data was collected through a structured approach as follows.

Questionnaire Administration
A standardized questionnaire was administered to all participants to gather demographic information and relevant medical history by direct face to face contact including the following data.

Demographics

- Age
- Gender
- Participant Number

Anthropometric Measurements

- Waist circumference: Using a flexible measuring tape, waist circumference was assessed at the midpoint between the lower rib and the iliac crest
- Height measurements were taken with a stadiometer, while weight was measured with a calibrated scale. The formula BMI = weight (kg)/height (m^2) was used to compute the Body Mass Index (BMI)

Lifestyle and Medical History

- Smoking
- History of thyroid disease
- Family history of thyroid disease
- Chronic drug user
- Neck surgery or irradiation

Vital Parameters

- Blood pressure was measured using a sphygmomanometer after the participant had rested for at least 5 minutes. Both systolic and diastolic pressures were recorded

Investigations
Each participant of the study from patient and control underwent the following investigation

Thyroid Function Tests

- Blood samples were drawn from participants to measure serum levels of Thyroid Stimulating Hormone (TSH), Free T4, and Free T3. These tests were performed using standard laboratory techniques(The LIAISON XL analyzer primarily uses chemiluminescence immunoassays (CLIA) for detection, specifically employing a sandwich assay format with magnetic microparticles)

Ultrasound of the Neck

- A qualified radiologist performed a neck ultrasound to evaluate the thyroid gland's structure. The ultrasound assessed the presence of nodules, goiter, or other abnormalities and measurements of the thyroid gland was be recorded

Lipid Profile

- A fasting blood sample was collected to measure serum levels of total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides. These were analyzed using standard enzymatic methods

Routine Laboratory Parameters

- Additional blood tests were performed including fasting glucose levels and liver function tests (e.g., ALT, AST, bilirubin) to rule out any underlying conditions that may affect thyroid function

Data Analysis

- The collected data was entered into an Excel spreadsheet for organization and preliminary analysis
- Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 22. Descriptive statistics (mean, standard deviation, frequency, and percentage) summarized the demographic and clinical characteristics of the participants
- Comparisons between the metabolic syndrome group and the control group was conducted using:
  - **Independent t-tests** for continuous variables (e.g., thyroid hormone levels, lipid profiles)
  - **Chi-square tests** for categorical variables (e.g., presence of thyroid nodules)
- A p-value of less than 0.05 was be considered statistically significant, indicating a meaningful difference between the groups

RESULTS

This study purposively included a total of 100 participants, evenly distributed between individuals with Metabolic Syndrome (n = 50) and those without (n = 50), to enable an attentive comparison of key metabolic and cardiovascular indicators. The result revealed statistically significant differences across several variables. Participants with Metabolic Syndrome had a higher mean waist circumference (105.5 cm vs. 98.45 cm, $p = 0.001$), elevated triglyceride levels (204.26 mg/dL vs. 120.84 mg/dL, $p<0.001$), and higher fasting blood sugar (118.44 mg/dL vs. 96.53 mg/dL, $p<0.001$). Additionally, HDL cholesterol was significantly lower in the Metabolic Syndrome group (41 mg/dL vs. 46.59 mg/dL, $p = 0.006$), and systolic blood pressure was notably higher (133.3 mmHg vs. 122.86 mmHg, $p<0.001$). These findings align with the clinical criteria for Metabolic Syndrome and highlight the clustering of risk factors that contribute to increased cardiometabolic risk, as shown in Table 1.

Table 1: Frequency Distribution Table of the Participants

Variable	Metabolic Syndrome	N	Mean	Std. Deviation	t-test for Equality of Means		
					df	Sig. (2-tailed)	Mean Difference
Age	Yes	50	52.68	14.281	97	0.061	5.251
	No	50	47.43	13.277			
Waist Circumference (cm)	Yes	50	105.5	11.68	97	0.001	7.051
	No	50	98.45	8.347			
TG (mg/dL)	Yes	50	204.26	96.482	97	<0.001	83.423
	No	50	120.84	44.958			
HDL (mg/dL)	Yes	50	41	9.837	97	0.006	-5.592
	No	50	46.59	10.05			
FBS (mg/dL)	Yes	50	118.44	28.915	97	<0.001	21.909
	No	50	96.53	7.848			
Systolic Blood Pressure (mmHg)	Yes	50	133.3	15.799	97	<0.001	10.443
	No	50	122.86	10.849			

FBS: Fasting Blood Sugar; HDL: High Density Lipoprotein; TG: Triglyceride

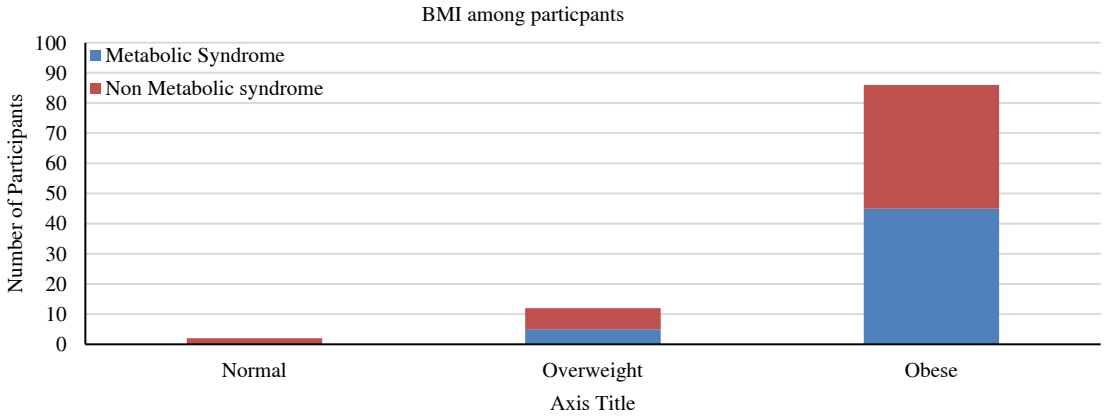

Figure 1: Participant Distribution by BMI

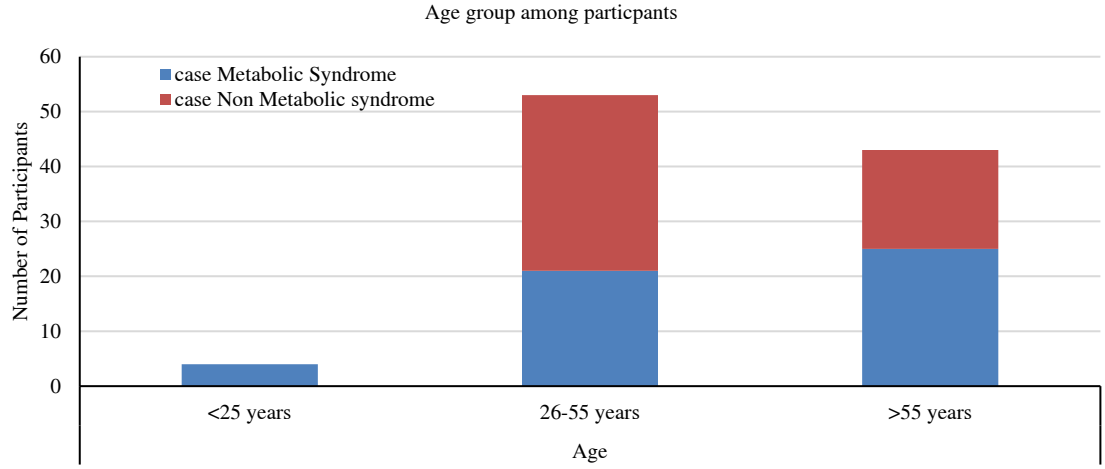

Figure 2: Participant Distribution by Age Group

The majority of participants 86% are classified as obese, while only a small fraction 2% have a normal weight as shown in Figure 1.

More than half of the participants, 53%, are aged between 26 and 55, indicating that this age group is the most represented. Only a small percentage (4%) are under 25 years old. There is a higher representation of male, 53%, compared to females, 47%. As shown in Figure 2 and 3.

Table 2 illustrates the distribution of thyroid abnormalities among participants with and without metabolic syndrome.

Among those with metabolic syndrome (n = 50), the majority were euthyroid (58%), followed by hypothyroidism (30%), sub-clinical hypothyroidism (10%), and subclinical hyperthyroidism (2%).

In contrast, among participants without metabolic syndrome (n = 50), a higher proportion were euthyroid

Table 2: Distribution of Thyroid Abnormalities in Individuals with and without Metabolic Syndrome

Thyroid Abnormality	Metabolic Syndrome (n = 50)	Non-Metabolic Syndrome (n = 50)	Total (n = 100)
Euthyroid	29 (58.0%)	39 (78.0%)	68 (68.0%)
Hypothyroidism	15 (30.0%)	5 (10.0%)	20 (20.0%)
Sub-clinical Hypothyroidism	5 (10.0%)	5 (10.0%)	10 (10.0%)
Subclinical Hyperthyroidism	1 (2.0%)	1 (2.0%)	2 (2.0%)
p-value	0.008		

Table 3: Thyroid Nodule Distribution by Metabolic Syndrome Status

Group	Thyroid Nodule	Non nodular	Total	p-value
Metabolic Syndrome	18 (36.0%)	32 (64.0%)	50	0.0044
Non-Metabolic Syndrome	5 (10.0%)	45 (90.0%)	50	
Total	23 (23.0%)	77 (77.0%)	100	

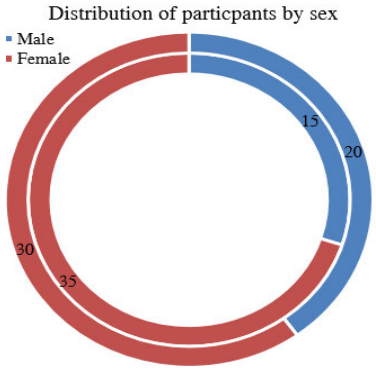

Figure 3: Participant Distribution by Sex

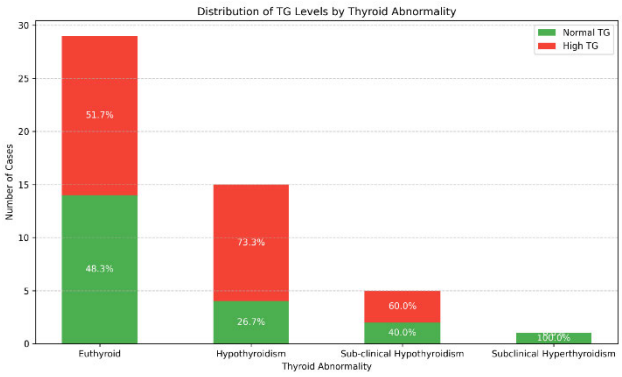

Figure 4: Proportion and Association of Thyroid Abnormality with Serum TG Level Among Metabolic Cases

(78%), with lower occurrences of hypothyroidism (10%), sub-clinical hypothyroidism (10%), and subclinical hyperthyroidism (2%).

The statistical analysis yielded value of 0.008, indicating a significant association between thyroid status and the presence of metabolic syndrome.

This study shows that among individuals with metabolic syndrome (50 studied cases) there is a trend of increased high TG levels in individuals with hypothyroid conditions, especially clinical hypothyroidism, compared to those with normal thyroid function. In figure 4 we see elevated serum triglyceride levels observed at 73.3% of cases with hypothyroidism, 60.0% of cases with subclinical hypothyroidism, and 51.7% of euthyroid cases. The difference in triglyceride levels across thyroid dysfunction groups was statistically significant (p = 0.02). This suggests a possible association between thyroid dysfunction and elevated triglycerides, particularly in hypothyroid states.

Among the 50 individuals with metabolic syndrome, 18(36%) was found to have thyroid nodules, compared to only 5(10%) among those without metabolic syndrome. A statistically significant association was observed between metabolic syndrome and the presence of thyroid nodules (χ^2 = 8.13, p = 0.0044, df = 1). The higher proportion of thyroid nodules in the metabolic syndrome group suggests that this distribution is unlikely to be due to chance, as shown in Table 3.

DISCUSSION

The aim of this study was to show the available proof on the association between metabolic syndrome, its components, and incidence of thyroid abnormalities. We found that thyroid abnormalities were more frequent in patients with metabolic syndrome in comparison to non-metabolic cases (42 and 22%). These findings are consistent with studies that found increased prevalence of thyroid disfunction among patients with metabolic syndrome [22-24]. However, there are a few studies that have assessed the inverse association, i.e., whether metabolic syndrome at baseline increases the risk of developing thyroid disease [25]. In our study we found that the reverse is also true; there is a clear association between metabolic syndrome and thyroid dysfunction particularly subclinical and overt hypothyroidism. A study by Jayakumar [26] found that out of 120 patients who were diagnosed with metabolic syndrome, thyroid functions were normal in 48 patients. Hypothyroidism and subclinical hypothyroidism were present in 60% of patients with metabolic syndrome. Another study by Ogbera et al. in Nigeria showed the proportion of subjects with hypothyroidism, euthyroid and hyperthyroidism who had metabolic syndrome, was 40.0, 42.0 and 24.0%, respectively [27]. These findings reinforce the bi-directional relationship between these conditions. In addition, there was a significant difference noted among the serum triglyceride levels of the participants, with the hypothyroid patients exhibiting higher levels. It is well known that thyroid hormones play an important role in lipid metabolism and clearance [10]. The observed association in our study aligns with evidence reporting the association between hypertriglyceridemia and hypothyroidism [28]. Interestingly, animal studies by Han and colleagues revealed that excess of iodine combined with

fatty diet could lead to damage to thyroid glands and thyroid dysfunction in mice [29]. This could explain our findings of increased thyroid nodules in patients with metabolic syndrome. This association is also demonstrated by a study done by Li *et al.* [30]. Several mechanisms may be responsible for this association. Insulin resistance, which is a key component of metabolic syndrome, can stimulate the proliferation of thyroid cells through insulin and insulin-like growth factors [31]. This could potentially explain the increased prevalence o of thyroid nodules. Moreover, adipokines such as leptin could adversely impact the hypothalamic-pituitary-thyroid axis, causing alterations in TSH secretion [32].

From a clinical standpoint, the findings of this study underscore the importance of performing thyroid evaluation in patients with metabolic syndrome to aid early detection and management of conditions that may be subclinical yet contribute to adverse cardiovascular outcomes [16]. Integrating thyroid function testing into metabolic syndrome management guidelines could therefore aid in improving risk stratification and developing preventative strategies particularly in Iraq, where prevalence of obesity, cardiovascular disease, and diabetes is on the rise [33].

CONCLUSIONS

This study demonstrated a higher prevalence of thyroid abnormalities, particularly hypothyroidism and thyroid nodules, among metabolic syndrome patients. Elevated serum triglycerides were also more strongly associated with thyroid dysfunction, highlighting a potential link between metabolic and endocrine dysfunction. Clinically, these findings mean that routinely performing thyroid function testing and ultrasound in patients with metabolic syndrome would be vital for better metabolic control and optimization of overall health. Future studies in the field should focus on a larger sample size taken from multiple settings in order to truly scope the effects of these conditions. Interventional studies are needed to assess whether treating thyroid dysfunction in metabolic syndrome improves outcomes.

Limitations

This study has several limitations. Its cross-sectional design will not establish causality. The sample size is relatively small and limited to a single center, which may affect generalizability. Second, there is potential for selection bias and reliance on self-reported data, which could introduce inaccuracies. Third, some confounding factors may have been missed despite exclusion criteria. Fourth, the short data collection period limits understanding of long-term changes.

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